

Recent advances in the management of hypertension

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Abstract

Recently, there have been several reports related to the adequacy of blood pressure (BP) control in high-risk hypertensive patients. These aspects have been reviewed in the recently published reappraisal of the European Society of Hypertension guidelines, and this short review comments on and briefly extends the discussion of this situation. In summary, a low BP goal when cardiorenal disease is advanced can be risky. However, attaining normal BP levels at earlier stages in the cardiorenal continuum is probably totally adequate.

Introduction and context

The latest evidence supported by the most recent comparative trials [1-6] has prompted a reconsideration of the current guidelines for the management of hypertension [7]. Consensus over the initiation of antihypertensive treatment and blood pressure (BP) goals is essential in order to optimize hypertension management and outcomes. In addition, BP measurement methods must be tested in order to establish the optimal and most reliable approach for determining accurate BP levels. Current recommendations are based on the finding that a given difference in BP, as measured in the clinic, results in a given difference in outcome, as demonstrated by observational and interventional studies and their meta-analyses [8-10].

Recent advances

Guidelines recommend the use of antihypertensive drugs in patients with grade 1 hypertension at low or moderate cardiovascular (CV) risk – namely, when systolic BP (SBP) is between 140 and 159 mm Hg or when diastolic BP is between 90 and 99 mm Hg (or when both occur) – provided that non-pharmacological treatment has proven ineffective. Nevertheless, there is inconclusive evidence of whether older persons with grade 1 hypertension, diabetics, or patients with coronary disease and high normal BP should be treated [7]. Therefore, ongoing and future trials are necessary to set

up a more robust assessment of treatment benefits in these patients (Table 1). Also, discussion about the most adequate BP goals is emerging from a number of recent studies. It seems reasonable, particularly given the results of a number of prospective trials, that SBP should be reduced to less than 140 mm Hg in the general population of patients with grade 1 or 2 hypertension and low or moderate total CV risk. Information on BP thresholds and targets for drug treatment has also resulted from *post hoc* analyses of event-based trials and from studies on the effects of treatment on organ damage of prognostic importance, although, admittedly, this is weaker evidence. In the ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial (ONTARGET) [3], favorable effects of BP reductions were seen when initial SBP values were above 140 mm Hg, even after adjusting for potential confounders, and a greater BP reduction was usually accompanied by greater CV protection. Conversely, the benefit was less obvious and primarily limited to stroke patients in whom initial SBP was in the range of 130 mm Hg [11]. The lack of benefit observed in this trial was directly related to the high CV risk of the population included. Consequently, the recommendation of previous guidelines to aim for a lower SBP goal (<130 mm Hg) in patients at very high CV risk may be prudent but is not consistently supported by trial evidence. In no randomized trial in diabetic patients has SBP been reduced to below 130 mm Hg with

Table 1. Consensus in treatment initiation [7]

1. Although trial evidence is scanty, it appears reasonable to recommend that, in grade 1 hypertensives (systolic blood pressure [SBP] of 140-159 mm Hg or diastolic blood pressure [DBP] of 90-99 mm Hg) at low or moderate risk, drug therapy should be started after a suitable period with lifestyle changes. A more prompt initiation of treatment is advisable if grade 1 hypertension is associated with a high level of risk or if hypertension is grade 2 or 3.
2. In patients with high normal blood pressure (BP) (SBP of 130-139 mm Hg or DPB of 85-89 mm Hg) uncomplicated by diabetes or previous cardiovascular events, no trial evidence of treatment benefits, except for a delayed onset of hypertension (crossing the 140/90 mm Hg cutoff) is available.
3. Initiation of antihypertensive drug therapy in diabetic patients with high normal BP is currently unsupported by prospective trial evidence. For the time being, it appears prudent to recommend treatment initiation in high normal BP diabetic patients if subclinical organ damage (particularly microalbuminuria or proteinuria) is present.
4. Trial evidence concerning antihypertensive drug treatment in patients with previous cardiovascular events in the absence of hypertension is controversial, and further trials must be completed before firm recommendations can be given.
5. Early BP-lowering treatment, before organ damage develops or becomes irreversible or cardiovascular events occur, appears to be a prudent recommendation.

Table 2. Consensus in blood pressure goals of treatment [7]

1. On the whole, there is sufficient evidence to recommend that systolic blood pressure (SBP) be lowered to below 140 mm Hg (and diastolic blood pressure [DBP] to below 90 mm Hg) in all hypertensive patients, both those at low moderate risk and those at high risk. Evidence is missing only in older hypertensive patients, in whom the benefit of lowering SBP to below 140 mm Hg has never been tested in randomized trials.
2. The recommendation of previous guidelines to aim for a lower SBP goal (<130 mm Hg) in diabetic patients and in patients at very high cardiovascular risk (previous cardiovascular events) may be wise, but it is not consistently supported by trial evidence. In no randomized trial in diabetic patients has SBP been reduced to below 130 mm Hg with proven benefits, and trials in which SBP was lowered to below 130 mm Hg in patients with previous cardiovascular events have produced controversial results.
3. Despite their obvious limitations and a lower strength of evidence, *post hoc* analyses of trial data indicate a progressive reduction of incidence of cardiovascular events with progressive lowering of SBP to about 120 mm Hg and DBP to about 75 mm Hg, although the additional benefit at low BP values becomes rather small. A J-curve phenomenon is unlikely to occur until lower values are reached, except perhaps in patients with advanced atherosclerotic artery diseases.
4. On the basis of current data, it may be prudent to recommend lowering SBP/DBP to values within the range of 130-139/80 to 85 mm Hg (in particular, to lower values in this range) in all hypertensive patients. However, additional critical evidence from specific randomized trials is desirable.

proven benefits, and trials in which SBP was lowered to below 130 mm Hg in patients with previous CV events have produced controversial results (Table 2).

Finally, a close analysis of most of the relevant trials suggests that the absence of benefit of antihypertensive therapy in some trials might be due to the fact that some patients have normal BP at trial entry. Enrollment of patients into clinical trials on the basis of office-based BP alone might no longer be appropriate. An increasing amount of data is coming from clinical trials that include patients who are evaluated by ambulatory monitoring of BP [12-14]. The results of these studies may allow a better assessment of trial eligibility. Moreover, they identify the individuals with the lowest actual BP, who thus are at higher risk of adverse effects of treatment.

Implications for clinical practice

The question of whether trials should include ambulatory BP monitoring and home BP monitoring as well as conventional clinic measurements must be answered in upcoming trials. Ambulatory BP values are known to correlate with organ damage and CV events better than clinic measurement does [15]. However, ambulatory BP monitoring is not widely employed in trials, and when it is employed, it is in a minor subgroup of patients only. So far, when ambulatory BP was measured, the correlation between the antihypertensive effect measured by

ambulatory and office BP appears to be quite different. The proportion of hypertensive patients achieving satisfactory BP control also differs depending on whether BP is measured in the clinic or by ambulatory monitoring. Comparative data are few and show discrepant results: some controlled studies indicate an easier BP control by clinic measurement (<140/90 mm Hg) than by ambulatory BP monitoring (<130/80 mm Hg) [16], whereas Spanish registry data [12,17] suggest that almost half of all patients with office-diagnosed hypertension are normotensive when assessed by ambulatory BP monitoring. Hence, future trials should use ambulatory BP monitoring alongside conventional clinic BP measurements.

Abbreviations

BP, blood pressure; CV, cardiovascular; SBP, systolic blood pressure.

Competing interests

The authors declare that they have no competing interests.

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